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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,423	02/08/2002	Minutza Leibovici	1662/51303	1722

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EXAMINER	
LANDAU, SHARMILA GOLLAMUDI	
ART UNIT	PAPER NUMBER
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/071,423	LEIBOVICI ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9-18,20-28,30,32-35,39 and 43-74* is/are pending in the application.

4a) Of the above claim(s) *1,16-18,20-28,30,32-35,39 and 43-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-6, 9-15, and 50-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Request for Continued Examination and Amendments/Arguments received on 6/14/06 is acknowledged. Claims **1-6, 9-18, 20-28, 30, 32-35, 39, and 43-74** are pending in this application.

Election/Restrictions

Applicant's election with traverse of Group II, claims 2-6, 9-15, and 50-74, in the reply filed on 2/7/07 is acknowledged. The traversal is on the ground(s) that the search would not be undue burden. This is not found persuasive because restriction between a product and process of making if it can be shown that the process claimed can make a materially different product or if the product can be made by another process. As set forth in the Restriction Requirement the process of making, invention I, makes a materially different product, a highly purified torsemide modification II, whereas the invention II only claims torsemide modification II without limiting its purity. Therefore, the search for invention I does not necessarily encompass a search for invention I. Therefore, claims 2-6, 9-15, and 50-74 are directed to the elected invention and claims 1, 16-18, 20-28, 30, 32-35, 39, 43-49 are withdrawn as being directed to the non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

Response to Arguments

Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 9, 11-15, and 50-51 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of the amendments of 6/14/06.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 9-18, 50-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a stable pharmaceutical composition comprising torsemide modification II with no trace amounts of modification I (high purity torsemide modification II, wherein no more than 15% torsemide II does not rearrange into another form during storage for at least 3 months, does not reasonably provide enablement for applicant is not enabled for a stable pharmaceutical composition comprising torsemide modification II with trace amounts of modification I, wherein no more than 15% torsemide II does not rearrange into another form during storage for at least 3 months. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Enablement is considered in the view of the Wands factors (MPEP 2164.01 (a)). These include the nature of the claims, guidance of the specification, the existence of working

examples, predictability of the prior art, and state of the prior art. All of the Wands factors have been considered with the regard to the instant claims, with the most relevant discussed below. The instant claims are not enabled to prevent healing of the skin indefinitely and the process of treatment by prevention of healing.

Nature of the Invention: The rejected claims are drawn to a stable pharmaceutical formulation containing torsemide modification II wherein no more than 15% torsemide II does not rearrange into another form during storage for at least 3 months.

Breath of the claims: The breadth of the claim encompasses maintaining stability of torsemide modification II for at least 3 months using torsemide modification II with trace amount of torsemide modification I.

Guidance of the Specification: The guidance provided by the specification on page 5 discloses high purity torsemide modification II, with no trace amount of torsemide modification I, is stable during storage under stress conditions for at least 3 months. The specification also discloses: "In contrast, torsemide modification II that contains trace amounts of torsemide modification I is not stable during storage under stress condition for at least 3 months." The torsemide modification II containing trace amounts of torsemide modification I rearranges into torsemide modification I over time during storage under stress conditions.

The State of the Art: The state of the art recognizes the instability of torsemide modification II and that it rearranges into modification I within 10 to 14 days. See RE 34,672, column 2.

Working Examples: The examples in the specification demonstrate that high purity torsemide modification I is stable for stable for at least three months. However, Table 4

demonstrates that a composition with torsemide modification II with trace amount of modification I does undergo rearrangement.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-6, 9-15, and 50-74 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,482,417. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Instant application claims a stable pharmaceutical composition high purity torsemide modification II that does not rearrange over time for at least three months. Further, the dependent claims recite particle sizes of 200, 100, and 50 microns.

US patent claims a pharmaceutical composition comprising torsemide modification that does not rearrange over time. The dependent claims recite a stable product that does not rearrange over time at least for three months. Further the dependent claims recite particles sizes of 200, 100, and 50 microns. The stable pharmaceutical formulation of claim 1, wherein said

formulation further comprises lactose anhydrous, crospovidone, povidone, cellulose, and magnesium stearate.

Therefore, both instant application and US '417 are directed to similar subject matter.

Response to Arguments

Applicant states that a terminal disclaimer will be filed when the claims are found to be allowable.

The rejection is maintained until a Terminal Disclaimer if filed.

Claims 2-6, 9-18, 52-74 are under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 81-82, 85-87 U.S. Patent No. 6,465,496 in view of Topfmeier et al (RE 34, 672). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Instant application claims a high purity torsemide modification II. The dependent claims recite a stable product that does not rearrange over time for at least three months. Further, the dependent claims recite particle sizes of 200, 100, and 50 microns.

US '496 claims a pharmaceutical composition comprising torsemide Dupont Form 2 (torsemide modification II) and a pharmaceutically acceptable carrier and a method of treating edema.

US '496 does not claim the specific excipient.

However, Topfmeier et al teach a stable pharmaceutical composition comprising torsemide I with conventional excipients such as sugars, cellulose, and lubricating agents. Specifically, magnesium stearate is taught. See examples. RE 34, 672 teaches the instant particles ranges and the instant rate of dissolution on column 3, lines 10-15.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the instant excipients and arrive at the instant invention. One would have been motivated to do so with a reasonably expectation of success since Topfmeier et al teach the use of conventional additives such as the instantly claimed excipients for stable pharmaceutical compositions containing torsemide modification I and II respectively.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2-6, 9-18, 52-74 are rejected under 35 U.S.C. 102(e) as being anticipated by Aronhime et al (6,465,496).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Aronhime et al discloses torsemide polymorphs. The reference discloses the process of preparing torsemide modification II. Note column 10, lines 10 to column 11, line 12. The new forms of torsemide are incorporated into pharmaceutically acceptable carriers and excipients known in the art. The dosage amount is about 2 to 200 mg per day and preferably 5 to 100 mg per day. See column 10, lines 46-60. The disclosure of RE 34,672 is incorporated into the

disclosure of Aronhime et al. RE 34, 672 discloses the instant particles ranges and the instant rate of dissolution on column 3, lines 10-15. Further RE 34,672 discloses magnesium stearate as an excipient in the examples.

The process of making high purity torsemide modification II involves:

Example 9 discloses preparing torsemide modification I by placing torsemide modification II and acetonitrile: water mixture and isolating torsemide modification II. This step reads on instant limitation (a) and (b).

Example 12 discloses placing torsemide modification I in water and adjusting the pH of the solution to 10.2 +/- 0.2 with 20% NaOH. This step reads on instant limitation (c) and (d). The solution is then filtered and the pH is adjusted to a pH of 6.25 +/- 0.2. This step reads on instant limitation (e) and (f). The precipitate is filtered washed and torsemide modification II is isolated.

With regard to the high purity torsemide modification II product claims, it is the examiner's position that the stability limitations are inherent since both the prior art and the applicant utilize the same process of making high purity modification II (this is substantiated by applicant's disclosure on page 11); therefore the prior art's pharmaceutical composition will also have the same properties as the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dreckmann-Behrendt (5,914,336) in view of Topfmeier et al (RE 34, 672).

Dreckmann-Behrendt teach a pharmaceutical composition comprising 10% of torsemide II and 45% of a mixture of torsemide modification I and III. see example 5. The reference teaches the use of excipients such as sugars, cellulose, and lubricating agents, known in the art, for an instant release oral tablet. Further, Dreckmann-Behrendt teaches the particle size of torsemide. (Note col. 3, lines 43-58). The reference teaches different doses (2.5 mg to 200 mg) according to dosage form and the use of torsemide as a diuretic and treatment of edema (col. 4, lines 35-60).

Although Dreckmann-Behrendt teaches the use of cellulose, US '336 does not specify the type of cellulose, i.e. microcrystalline cellulose, or specify the lubricating agent or sugar.

Topfmeier et al teach a stable pharmaceutical composition comprising torsemide I with excipients such as sugars, cellulose, and lubricating agents. Specifically, magnesium stearate is taught. See examples.

It would have been obvious to one of ordinary skill in the art at the time the invention was made combine the teachings of Dreckmann-Behrendt and Topfmeier et al and utilize the instant excipients. One would have been motivated to do so with a reasonably expectation of success since Topfmeier et al teach the use of conventional additives such as the instantly claimed excipients for stable pharmaceutical compositions containing torsemide I and Dreckmann-Behrendt teach a composition comprising torsemide I.

Conclusion

All the claims remain rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharmila S. Gollamudi
Primary Examiner
Art Unit 1616

SSG